

A New *cine*-Substitution of Alkenyl Sulfones with Aryltitanium Reagents Catalyzed by Rhodium: Mechanistic Studies and Catalytic Asymmetric Synthesis of Allylarenes

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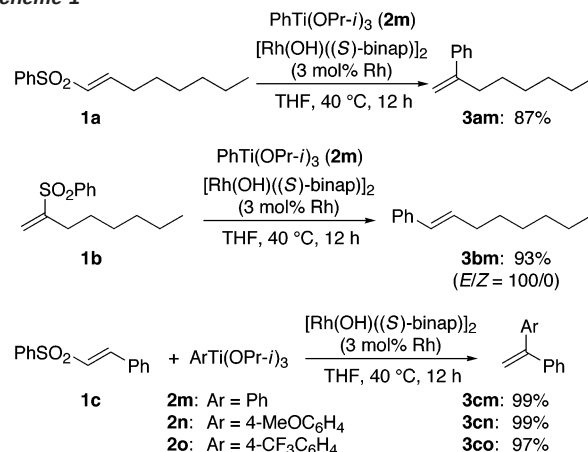
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The *cine*-substitution reaction has attracted considerable attention as a result of its rather unusual substitution pattern and its synthetic utility.¹ It takes place mostly in aromatic systems, and only a few types have been reported on the *cine*-substitution in nonaromatic systems, the representatives being those observed as competing side reactions in palladium-catalyzed cross-couplings of alkenylstannanes and -silanes.² On the other hand, we have reported the rhodium-catalyzed asymmetric addition of organoboron^{3,4} and -titanium⁵ reagents to various types of electron-deficient olefins which proceeds through carbo-rhodation of the olefins as a key step, giving the corresponding 1,4-addition products with high enantioselectivity. On using alkenyl sulfones⁶ as substrates for the rhodium-catalyzed addition of organometallic reagents, we found a new type of *cine*-substitution where the sulfonyl group is eliminated after the carbo-rhodation step.⁷ Here we wish to report the catalytic *cine*-substitution reaction, its catalytic cycle established by deuterium-labeling studies and its application to catalytic asymmetric synthesis of allylarenes with over 99% enantioselectivity.

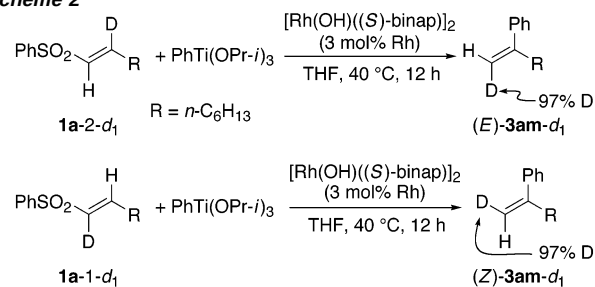
In the first set of experiments, a pair of regioisomeric alkenyl sulfones, (*E*)-1-phenylsulfonyl-1-octene (**1a**) and 2-phenylsulfonyl-1-octene (**1b**), were allowed to react with phenyltitanium triisopropoxide (PhTi(OPr-*i*)₃)⁸ (**2m**) in the presence of 3 mol % of [Rh(OH)((*S*)-binap)]₂^{3j} in THF at 40 °C for 12 h (Scheme 1). The reaction of **1a** gave 87% yield of 2-phenyl-1-octene (**3am**), and that of **1b** gave 93% yield of (*E*)-1-phenyl-1-octene (**3bm**) with perfect regioselectivity in both reactions. Thus, *cine*-substitution where the phenylsulfonyl group is substituted with the phenyl group on the next carbon took place in both regioisomeric alkenyl sulfones **1a** and **1b**. The *cine*-substitution was also observed in the reaction of (*E*)-1-phenylsulfonyl-2-phenylethene (**1c**) with PhTi(OPr-*i*)₃ (**2m**) and those containing an electron-donating or -withdrawing group on the phenyl **2n,o**, which gave the corresponding substitution products **3cm**, **3cn**, and **3co**, respectively, in a quantitative yield. With organoboron reagents such as phenyl-9BBN or triphenylcycloboroxane ((PhBO)₃) in place of the aryltitanium reagents, neither this type of *cine*-substitution nor the 1,4-addition took place.

Deuterium-labeling experiments shown in Scheme 2 gave us an insight into the mechanism of the present *cine*-substitution. The rhodium-catalyzed reaction of (*E*)-2-deuterio-1-phenylsulfonyl-1-octene (**1a-2-d₁**) (99% D) with PhTi(OPr-*i*)₃ (**2m**) gave (*E*)-1-deuterio-2-phenyl-1-octene ((*E*)-**3am-d₁**) where the deuterium content at the *E* position is 97%. Consistent with this deuterium shift, the reaction of (*E*)-1-deuterio-1-phenylsulfonyl-1-octene (**1a-1-d₁**) (99% D) gave (*Z*)-1-deuterio-2-phenyl-1-octene ((*Z*)-**3am-d₁**) with the deuterium content of 97% at the *Z* position. Scheme 3 illustrates the formation of the *cine*-substitution product using for an example the reaction starting from **1a-2-d₁**. Addition of a phenyl-rhodium species⁵ to the alkenyl sulfone in a *syn* fashion generating alkyl-rhodium intermediate **A** followed by β-deuterium elimination with *syn* stereochemistry and readdition of the deuterium–rhodium

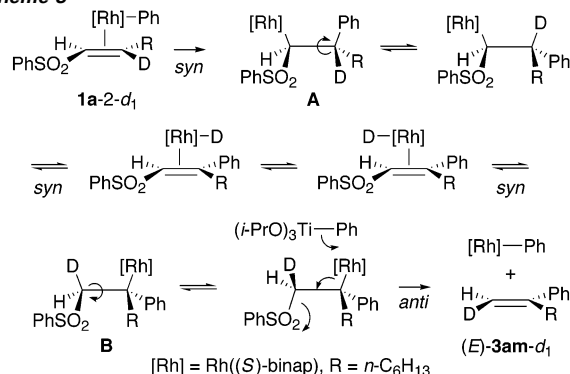
Scheme 1



Scheme 2

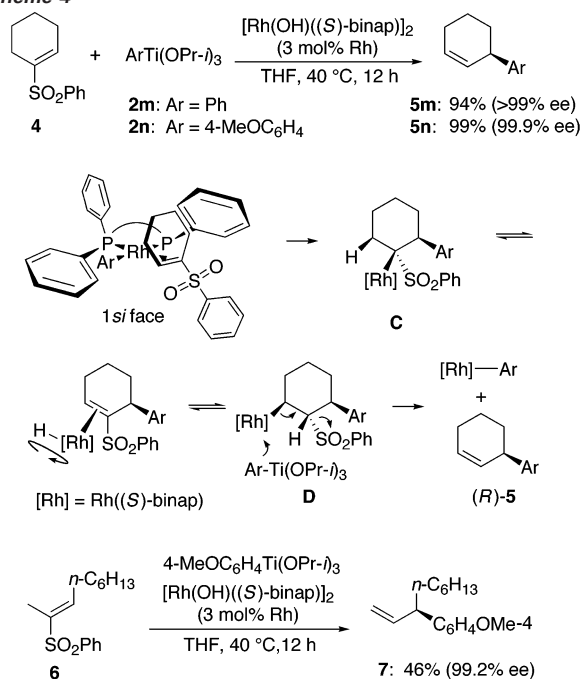


Scheme 3



to the double bond with *syn* stereochemistry and with opposite regiochemistry forms new alkyl-rhodium intermediate **B**. The last step, elimination of the sulfonyl group and the rhodium from **B**, should proceed in an *anti* fashion to give the *cine*-substitution product (*E*)-**3am-d₁** where the deuterium is at *E* position to the phenyl.⁹ It is likely that the last step consists of nucleophilic attack of the phenyltitanium on the rhodium and *E₂* elimination of the phenylsulfonyl as a leaving group.

Scheme 4



In the reaction of cyclic alkenyl sulfone, the asymmetric carbon center created at the carbo-rhodation step is retained in the substitution product (Scheme 4). Thus, the reaction of 1-phenylsulfonylcyclohexene (**4**) with $\text{PhTi}(\text{OPr-}i)_3$ (**2m**) in the presence of $[\text{Rh}(\text{OH})((S)\text{-binap})]_2$ gave 94% yield of (*R*)-3-phenylcyclohexene (**5m**) whose enantiomeric excess turned out to be over 99% ee by GC analysis with a chiral stationary phase column.¹⁰ The very high enantioselectivity (99.9% ee) was also observed in the reaction with $4\text{-MeOC}_6\text{H}_4\text{Ti}(\text{OPr-}i)_3$ (**2n**) giving the corresponding 3-aryl-cyclohexene (**5n**).^{11,12} The coordination of **4** to the (*S*)-binap/Rh with its 1*si* face at the insertion into the aryl-rhodium intermediate^{3a,c,e} leads to the *R* configuration of the substitution products **5**. Because the alkyl-rhodium intermediate **C** formed by the insertion does not have the *syn* β -hydrogen on the aryl-substituted carbon, the β -hydrogen elimination takes place for the *syn* β -hydrogen on the other neighboring carbon. Subsequent *syn* hydro-rhodation and the *anti* elimination from **D** produces the allylic arenes **5**.

The selective formation of allylic arene was also observed in the reaction of (*E*)-2-phenylsulfonyl-2-nonene (**6**) which is a sulfone of internal alkene. Although the yield was not high enough, the enantioselectivity forming allylarene **7** in the reaction with **2n** was surprisingly high (99.2% ee).¹³ For this alkenyl sulfone **6**, the hydrogen on the methyl carbon is abstracted at the β -hydrogen elimination on the alkyl-rhodium intermediate much more readily than that on the sterically congested carbon substituted with phenyl and hexyl groups, resulting in the selective formation of **7**.

In conclusion, we found a new type of *cine*-substitution reaction of alkenyl sulfones with aryltitanium reagents, which is catalyzed by a rhodium complex, and we established its catalytic cycle by

deuterium-labeling studies. In some cases, the catalytic asymmetric carbon-carbon bond formation was realized with high enantioselectivity (>99% ee).

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Supporting Information Available: Experimental procedures, spectroscopic and analytical data for the products (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (12) The reaction of 1-phenylsulfonylcyclopentene under the same conditions gave a lower yield (ca. 5%) of 3-phenylcyclopentene.
- (13) The enantiomeric purity was determined by HPLC analysis with chiral stationary phase column, Chiralcel OJ (hexane).

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